IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: James P. Elia	)	Group Art Unit: 1647
Serial No.: 10/179,589	)	Examiner: Daniel C. Gamett
Filed: June 25, 2002	)	
For: METHOD FOR GROWING HUMAN ORGANS AND SUBORGANS	)	

FOURTH SUPPLEMENTAL DECLARATION
OF RICHARD HEUSER, M.D., F.A.C.C., F.A.C.P.

I Richard Heuser declare as follows:

1. I have offices at 555 N. 18th Street, Suite 300, Phoenix, Arizona 85006.

2. My Curriculum Vitae was attached as Exhibit A to my Declaration of November 16, 2004. Paragraph 3 of my Declaration and my Supplemental Declaration of February 15, 2005 provide additional information regarding my background and experience.

3. I have read and understood the disclosures of the above-referenced patent application Serial No. 10/179,589 at page 4, line 1 through page 5, line 14; at page 13, lines 3-10; at page 22, line 5 through page 24, line 15; and at page 26, line 3 through page 27, line 3. A copy of such disclosures was attached as Exhibit B to my Third Supplemental Declaration dated April 20, 2007. It is my understanding that the same disclosure is found in co-pending patent application. Serial No. 11/986,690. It is my further understanding that the same disclosures mentioned above are found at different pages and line numbers in the

specifications of co-pending patent application Serial Nos. 09/794,456; 09/836,750; 09/064,000; and 11/891,456.

I have also read and understood additional disclosures of the above-referenced patent application Serial No. 10/179,589 at page 9, lines 14-16; page 17, line 1 through page 20, line 8; page 21, lines 23 and 24; page 27, lines 1-3; page 28, lines 12-16; page 32, line 20 through page 39, line 19; and page 44, lines 8-17. A copy of such additional disclosures was attached as Exhibit C to my Third Supplemental Declaration dated April 20, 2007. It is my understanding that the same disclosure is found in co-pending patent application. Serial No.11/986,690. It is my further understanding that the same disclosures mentioned above are found at different pages and line numbers in the specifications of co-pending patent application Serial Nos. 09/794,456; 09/836,750; 09/064,000; and 11/891,456.

4. I note that the disclosures referenced in above Paragraph 3 relate to using a growth factor for promoting the growth of soft tissue, and more specifically, to a method of using a cellular growth factor, such as a stem cell, to grow an artery and/or cardiac muscle.

5. I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit A and have been informed that such claims will be presented in the above-referenced patent application Serial No. 10/179,589.

I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit B and have been informed that such claims are pending in co-pending application Serial No. 11/986,690.

I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit C and have been informed that such claims are pending in co-pending application Serial No. 09/794,456.

I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit D and have been informed that such claims are pending in co-pending application Serial No. 09/836,750.

I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit E and have been informed that such claims are pending in co-pending application Serial No. 09/064,000.

I have read and understood the claims set forth in the attached Fourth Supplemental Declaration Exhibit F and have been informed that such claims are pending in co-pending application Serial No. 11/891,456.

6. Based upon above Paragraphs 3-5, it is and remains my opinion that one skilled in the medical arts, armed with the direction and knowledge in such paragraphs, would be able to practice the method set forth in attached Exhibits A-F without need for resorting to undue experimentation.

7. I understand from reading the claims mentioned in above Paragraph 5 that implanting a composition which promotes artery growth is required and that artery growth requires the formation of multiple tissue layers comprising at least endothelial and smooth muscle cells. I also understand that it was commonly known at the time of the Elia invention, April 21, 1998, that bone marrow comprise stem cells that are pluripotent in that they are capable of forming multiple tissue types. I further understand that it was known that bone marrow contains CD34+ endothelial progenitor cells and that the medical art is aware that

such cells are unipotent and only differentiate into endothelial cells. When only CD34+ endothelial progenitor cells are transplanted into a human patient, it is not possible to cause artery formation because CD34+ endothelial progenitor cells do not differentiate into smooth muscle cells. In my opinion, it is not possible to cause artery formation by implanting only CD34+ endothelial progenitor cells into a human patient.

8. I have read and understood the language "stem cells harvested from bone marrow" as defined in the written disclosures above-mentioned patent applications and claims to encompass the entire population of bone marrow mononuclear cells and cellular components, including a range of cytokines, in contrast with any fractionated population of such cells. It is my understanding that as of circa the date of the Elia invention those skilled in the medical arts did not limit the scope of the term bone marrow stem cells to a subset of mononuclear cells composed of CD34+ endothelial progenitor cells. It is my opinion that one skilled in the medical arts reading the application at the time of filing, April 21, 1998, would have understood that the language was intended to describe a composition comprised of the entire population of bone marrow cellular components. To conclude otherwise, specifically in the absence of explicit direction to conduct a fractionation of cells, would require such a skilled person to ignore the decades of use of such language in the medical arts, particularly in regard to the practice of treating patients with bone marrow transplants.

9. Declarant states that the above opinion was reached independently.

Declarant understands that (1) any willful false statements and the like made herein are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of the application or any patent issuing thereon, and (2) that all statements made of Declarant's own

knowledge are true and that all statements made on information and belief are believed to be true.

Further Declarant sayeth not.

Date: 1/17/10

Richard Heuser

EXHIBIT A

CLAIMS

Claim 161 — The method of claim 174, wherein said stem cell comprises a living stem cell harvested from bone marrow.

Claim 162 — The method of claim 161, wherein said bone marrow is from said patient.

Claim 163 — The method of claim 174, wherein said stem cell comprises a living stem cell harvested from blood.

Claim 164 — The method of claim 163, wherein said blood is from said patient.

Claim 165 — The method of claim 174, wherein said stem cell is obtained from cell culture techniques.

Claim 166 — The method of claim 174, wherein said stem cell is placed into soft tissue in said body.

Claim 167 — The method of claim 166, wherein said stem cell is injected into said soft tissue.

Claim 168 — The method of claim 161, wherein said stem cell is placed into soft tissue in said body.

Claim 169 — The method of claim 168, wherein said stem cell is injected into said soft tissue.

Claim 170 — The method of claim 174, wherein said stem cell comprises a pluripotent stem cell.

Claim 171 The method of claim 170, wherein said pluripotent stem cell is placed in a leg of said patient by injection.

Claim 172 The method of claim 174 further comprising determining blood flow through said artery.

Claim 173 The method of claim 174 further comprising observing said artery.

Claim 174 A method of growing and integrating a desired artery at a selected site in a body of a human patient comprising the steps of locally placing a stem cell in a body of a human patient and growing said desired artery which integrates itself into said body at said selected site.

Claim 175 The method of claim 174, wherein said desired artery is grown around a blocked leg artery to bypass said blocked leg artery.

Claim 176 The method of claim 175, wherein said desired artery is grown around a blocked leg artery to bypass said blocked leg artery.

Claim 177 The method of claim 175, wherein said cell is placed into a leg artery.

Claim 178 The method of claim 176, wherein said cell is injected into a leg artery.

Claim 179 The method of claim 174, wherein said desired artery is grown around an at least partially blocked coronary artery to bypass said at least partially blocked coronary artery.

Claim 180 The method of claim 175, wherein said desired artery is grown around an at least partially blocked coronary artery to bypass said at least partially blocked coronary artery.

Claim 181 The method of claim 174, wherein said cell is placed into cardiac muscle of said human patient.

Claim 182 The method of claim 175, wherein said cell is injected into cardiac muscle of said human patient.

Claim 183 The method of claim 174, wherein said cell is placed into a partially blocked coronary artery of said human patient.

Claim 184 The method of claim 175, wherein said cell is injected into a partially blocked coronary artery of said human patient.

Claim 185 A method of growing and integrating a desired artery at a leg of the body of a human patient comprising the steps of injecting a pluripotent stem cell into a wall of an at least partially blocked leg artery and growing an artery which integrates itself into said body at the site of injection and bypasses said at least partially blocked artery.

Claim 186 A method of growing and integrating a desired artery at a heart of the body of a human patient comprising the steps of injecting a pluripotent stem cell into a wall of an at least partially blocked coronary artery and growing an artery which integrates itself into said body at the site of injection and bypasses said at least partially blocked artery.

Claim 187 A method of growing and integrating a desired artery at a heart of the body of a human patient comprising the steps of injecting a pluripotent stem cell into cardiac muscle and growing an artery which integrates itself into said body at the site of injection.

EXHIBIT B

Claims in co-pending application Serial No. 11/986,690

CLAIMS

Claim 6 — A method of growing and integrating a desired artery at a selected site in a body of a human patient comprising the steps of locally placing a cell in a body of a human patient and growing said desired artery which integrates itself into said body at said selected site.

Claim 7 — The method of claim 6, wherein said cell is placed into soft tissue in said body.

Claim 8 — The method of claim 7, wherein said cell is injected into said soft tissue.

Claim 9 — The method of claim 6, wherein said cell comprises a pluripotent stem cell.

Claim 10 — The method of claim 9, wherein said pluripotent stem cell is placed in a leg of said patient by injection.

Claim 11 — The method of claim 6 further comprising determining blood flow through said artery.

Claim 12 — The method of claim 6 further comprising observing said artery.

Claim 13 The method of claim 7, wherein said desired artery is grown around a blocked leg artery to bypass said blocked leg artery.

Claim 14 The method of claim 8, wherein said desired artery is grown around a blocked leg artery to bypass said blocked leg artery.

Claim 15 The method of claim 13, wherein said cell is placed into a leg artery.

Claim 16 The method of claim 14, wherein said cell is injected into a leg artery.

Claim 17 The method of claim 7, wherein said desired artery is grown around an at least partially blocked coronary artery to bypass said at least partially blocked coronary artery.

Claim 18 The method of claim 8, wherein said desired artery is grown around an at least partially blocked coronary artery to bypass said at least partially blocked coronary artery.

Claim 19 The method of claim 7, wherein said cell is placed into cardiac muscle of said human patient.

Claim 20 The method of claim 8, wherein said cell is injected into cardiac muscle of said human patient.

Claim 21 The method of claim 7, wherein said cell is placed into a partially blocked coronary artery of said human patient.

Claim 22 The method of claim 8, wherein said cell is injected into a partially blocked coronary artery of said human patient.

Claim 23 A method of growing and integrating a desired artery at a leg of the body of a human patient comprising the steps of injecting a pluripotent stem cell into a wall of an at least partially blocked leg artery and growing an artery which integrates itself into said body at the site of injection and bypasses said at least partially blocked artery.

Claim 24 A method of growing and integrating a desired artery at a heart of the body of a human patient comprising the steps of injecting a pluripotent stem cell into a wall of an at least partially blocked coronary artery and growing an artery which integrates itself into said body at the site of injection and bypasses said at least partially blocked artery.

Claim 25 A method of growing and integrating a desired artery at a heart of the body of a human patient comprising the steps of injecting a pluripotent stem cell into cardiac muscle and growing an artery which integrates itself into said body at the site of injection.

Claim 26 The method of claim 6, wherein a gene is included with said cell.

Claim 27 The method of claim 26, wherein said cell contains a gene inserted in said cell.

EXHIBIT C

Claims in co-pending application Serial No. 09/794,456

CLAIMS

Claim 7 A method of repairing a dead portion of a pre-existing heart comprising the steps of: placing a growth factor at a selected area of a human patient; and forming a new artery thereby causing said dead portion of said heart to be repaired.

Claim 12 The method of claim 7, wherein said growth factor comprises a cell.

Claim 15 The method of claim 12, wherein said growth factor is placed in said patient by injection.

Claim 18 The method of claim 15, wherein said injection is intramuscular.

Claim 19 The method of claim 12, wherein said growth factor is placed in said patient by a carrier.

Claim 21 A method of repairing a damaged portion of a pre-existing heart comprising the steps of: placing a growth factor at a selected area of a human patient; and forming a new artery thereby causing said damaged portion of said heart to be repaired.

Claim 26 The method of claim 21, wherein said growth factor comprises a cell.

Claim 29 The method of claim 26, wherein said growth factor is placed in said patient by injection.

Claim 32 The method of claim 29, wherein said injection is intramuscular.

Claim 33 The method of claim 26, wherein said growth factor is placed in said patient by a carrier.

Claim 35 A method of repairing a dead portion of a preexisting heart comprising the steps of placing a living stem cell harvested from bone marrow at a selected area of a human patient and forming a new artery thereby causing said dead portion of said heart to be repaired.

Claim 36 The method of claim 35, wherein said living stem cell is placed in said patient by injection.

Claim 37 The method of claim 35, wherein said living stem cell is locally placed in said patient.

Claim 38 A method of repairing a damaged portion of a preexisting heart comprising the steps of placing a living stem cell harvested from bone marrow at a selected area of a human patient and forming a new artery thereby causing said damaged portion of said heart to be repaired.

Claim 39 The method of claim 38, wherein said living stem cell is placed in said patient by injection.

Claim 40 The method of claim 38, wherein said living stem cell is locally placed in said patient.

Claim 41 The method of claim 7, wherein said growth factor comprises a cell and said cell is placed adjacent to said dead portion of said heart.

Claim 42 The method of claim 21, wherein said growth factor comprises a cell and said cell is placed adjacent to said damaged portion of said heart.

Claim 43 The method of claim 41, wherein said cell comprises a stem cell.

Claim 44 The method of claim 43, wherein said stem cell is injected into said heart.

Claim 45 The method of claim 42, wherein said cell comprises a stem cell.

Claim 46 The method of claim 45, wherein said stem cell is injected into said heart.

Claim 53 The method of claim 7 further comprising calculating blood flow through said newly formed artery.

Claim 54 The method of claim 7 further comprising observing said newly formed artery.

Claim 55 The method of claim 21 further comprising calculating blood flow through said newly formed artery.

Claim 56 The method of claim 21 further comprising observing said newly formed artery.

Claim 57 The method of claim 35, wherein said bone marrow stem cells are harvested from the patient and are placed into the heart of the patient by injecting said stem cells at a site adjacent said dead portion.

Claim 58 The method of claim 38, wherein said bone marrow stem cells are harvested from the patient and are placed into the heart of the patient by injecting said stem cells at a site adjacent said damaged portion.

EXHIBIT D

Claims in co-pending application Serial No. 09/836,750

CLAIMS

Claim 236 A method of growing a new portion of a pre-existing heart comprising the steps of placing a growth factor in a body of a human patient and growing new cardiac muscle and growing a new artery in said heart.

Claim 238 The method of claim 236, further comprising repairing a dead portion of said heart.

Claim 239 The method of claim 236, further comprising repairing a damaged portion of said heart.

Claim 244 The method of claim 236, wherein said growth factor comprises a cell.

Claim 247 The method of claim 236, wherein said growth factor is placed in said patient by injection.

Claim 250 The method of claim 247, wherein said injection is intramuscular.

Claim 251 The method of claim 236, wherein said growth factor is placed in said patient by a carrier.

Claim 253 The method of claim 236, wherein said growth factor comprises a gene and a cell.

Claim 257 The method of claim 236, wherein said growth factor is locally placed in said body.

Claim 258 The method of claim 238, wherein said growth factor is locally placed in said body.

Claim 259 The method of claim 239, wherein said growth factor is locally placed in said body.

Claim 260 The method of claim 244, wherein said growth factor is locally placed in said body.

Claim 261 The method of claim 236, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 262 The method of claim 238, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 263 The method of claim 239, wherein said growth factor comprises living stem cells harvested from bone marrow.

Claim 268 The method of claim 262, wherein said stem cell is placed in said patient by injection.

Claim 269 The method of claim 263, wherein said stem cell is placed in said patient by injection.

Claim 270 The method of claim 258, wherein said growth factor comprises a cell and said cell is placed adjacent to said dead portion of said heart.

Claim 271 The method of claim 259, wherein said growth factor comprises a cell and said cell is placed adjacent to said damaged portion of said heart.

Claim 280 The method of claim 236 further comprising calculating blood flow through said newly grown artery.

Claim 281 The method of claim 238 further comprising calculating blood flow through said newly grown artery.

Claim 282 The method of claim 239 further comprising calculating blood flow through said newly grown artery.

Claim 283 The method of claim 236 further comprising observing said newly grown artery.

Claim 284 The method of claim 238 further comprising observing said newly grown artery.

Claim 285 The method of claim 239 further comprising observing said newly grown artery.

Claim 288 The method of claim 261, wherein said stem cells are harvested from bone marrow of said patient and are placed into the heart of the patient by injection.

Claim 289 The method of claim 268, wherein said stem cells are harvested from the patient and are placed into the heart of the patient by injecting said stem cells at a site adjacent said dead portion.

Claim 290 The method of claim 269, wherein said stem cells are harvested from the patient and are placed into the heart of the patient by injecting said stem cells at a site adjacent said damaged portion.

EXHIBIT E

Claims in co-pending application Serial No. 09/064,000

CLAIMS

Claim 403

A method for growing and integrating tissue consisting of desired soft tissue at a selected site in a body of a human patient wherein said desired soft tissue comprises a desired artery comprising the steps of:

(a) locally injecting stem cells into said body at said selected site;

(b) forming a bud at said selected site; and

(c) growing said desired artery from said bud wherein said artery integrates itself into said body of said human patient at said selected site.

Claim 404

The method of claim 403, wherein said selected site comprises a damaged site in a leg of said patient and said stem cells are injected intramuscularly.

Claim 405

The method of claim 403, wherein said selected site comprises a damaged site in a heart of said patient and said stem cells are injected intramuscularly.

Claim 407

The method of claim 403, wherein said stem cell comprises a living stem cell harvested from bone marrow.

Claim 408	The method of claim 407, wherein said bone marrow is from said patient.
Claim 409	The method of claim 403, wherein said stem cell comprises a living stem cell harvested from blood.
Claim 410	The method of claim 409, wherein said blood is from said patient.
Claim 411	The method of claim 403 further comprising determining blood flow through said desired artery.
Claim 412	The method of claim 403 further comprising observing said desired artery.

EXHIBIT F

Claims in co-pending application Serial No. 11/891,456

CLAIMS

Claim 6 A method for producing and integrating tissue consisting of a desired soft tissue at a selected site in a body of a human patient comprising:

(a) placing cells in said body of said human patient;

(b) forming a bud at said selected site in said body of said human patient; and

(c) growing said desired soft tissue which integrates itself into said body of said human patient from said bud.

Claim 7 The method of claim 6, wherein said cells are multifactorial and non-specific.

Claim 8 The method of claim 7, wherein said cells comprise stem cells.

Claim 9 The method of claim 6 further comprising forming a new artery.

Claim 10 The method of claim 7 further comprising forming a new artery.

Claim 11 The method of claim 6, wherein said soft tissue comprises mesodermal tissue.

Claim 12 The method of claim 6, wherein said soft tissue comprises an artery.

Claim 13 The method of claim 6, wherein said cells comprise stem cells.

Claim 14 The method of claim 13, wherein said soft tissue comprises an artery.

Claim 15 The method of claim 6, wherein said cells comprise pluripotent cells.

Claim 16 The method of claim 15, wherein said soft tissue comprises an artery.

Claim 17 The method of claim 15, wherein said cells comprise stem cells.

Claim 18 The method of claim 17, wherein said stem cells are multifactorial and non-specific.

Claim 19 The method of claim 6, wherein said cells are injected into said body.

Claim 20 The method of claim 6, wherein said cells are locally placed into said body.

Claim 21 The method of claim 20, wherein said cells comprise stem cells.

Claim 22 The method of claim 20, wherein said cells are injected intramuscularly.

Claim 23 The method of claim 21, wherein said stem cells are injected intramuscularly.

Claim 24 The method of claim 12 further comprising determining blood flow through said new artery.

Claim 25 The method of claim 12 further comprising observing said new artery.

Claim 26 The method of claim 23, wherein said selected site comprises a leg of said patient.

Claim 31 A method for growing and integrating tissue consisting of desired soft tissue at a selected site in a body of a human patient wherein said desired soft tissue comprises a desired artery comprising the steps of:

(a) locally injecting stem cells into said body at said selected site;

(b) forming a bud at said selected site; and

(c) growing said desired artery from said bud wherein said artery integrates itself into said body of said human patient at said selected site.

Claim 32 The method of claim 31, wherein said selected site comprises a damaged site in a leg of said patient and said stem cells are injected intramuscularly.

Claim 33 The method of claim 31, wherein said selected site comprises a damaged site in a heart of said patient and said stem cells are injected intramuscularly.

Claim 34 The method of claim 31, wherein said stem cell comprises a living stem cell harvested from bone marrow.

Claim 35 The method of claim 34, wherein said bone marrow is from said patient.

Claim 36 The method of claim 31, wherein said stem cell comprises a living stem cell harvested from blood.

Claim 37 The method of claim 36, wherein said blood is from said patient.

Claim 38 The method of claim 31 further comprising determining blood flow through said desired artery.

Claim 39 The method of claim 31 further comprising observing said desired artery.